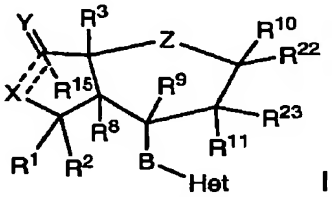
IN THE CLAIMS:

1. (Previously presented) A method of treating a therapeutic condition comprising administering to a mammal in need of such treatment an effective amount of at least one compound of the formula:



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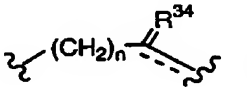
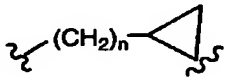
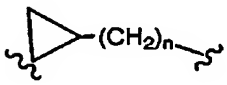
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof, wherein:

Z is $-(CH_2)_n-$,  ,  when R^{10} is absent, or  when R^3 is absent;

the single dotted line adjacent to R^{34} ====== represents an optional double bond;

the double dotted lines adjacent to X ====== together represent an optional single bond;

n is 0-2;

R^1 and R^2 are independently selected from the group consisting of H, C_1-C_6 alkyl, fluoro(C_1-C_6)alkyl, difluoro(C_1-C_6)alkyl, trifluoro-(C_1-C_6)alkyl, C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, aryl(C_1-C_6)alkyl, aryl(C_2-C_6)alkenyl, heteroaryl(C_1-C_6)alkyl, heteroaryl(C_2-C_6)alkenyl, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino-(C_1-C_6)alkyl, aryl and thio(C_1-C_6)alkyl; or R^1 and R^2 together form a =O group;

R^3 is H, hydroxy, C_1-C_6 alkoxy, $-NR^{18}R^{19}$, $-SOR^{16}$, $-SO_2R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{18}R^{19}$, C_1-C_6 alkyl, halogen, fluoro(C_1-C_6)alkyl, difluoro(C_1-C_6)alkyl, trifluoro(C_1-C_6)alkyl, C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, aryl(C_1-C_6)alkyl, aryl(C_2-C_6)alkenyl, heteroaryl(C_1-C_6)alkyl, heteroaryl(C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl,

amino(C_1-C_6)alkyl, aryl, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl or (C_1-C_6)alkylamino(C_1-C_6)alkyl;

R^{34} is (H, R^3), (H, R^{43}), =O or =NOR^{17} when the optional double bond adjacent to R^{34} is absent; R^{34} is R^{44} when the double bond is present;

Het is a mono-, bi- or tricyclic heteroaromatic group of 5 to 14 atoms comprised of 1 to 13 carbon atoms and 1 to 4 heteroatoms independently selected from the group consisting of N, O and S, wherein a ring nitrogen can form an N-oxide or a quaternary group with a C_1-C_4 alkyl group, wherein Het is attached to B by a carbon atom ring member of Het, and wherein the Het group is substituted by 1 to 4 moieties, W, independently selected from the group consisting of H; C_1-C_6 alkyl; fluoro(C_1-C_6)alkyl; difluoro(C_1-C_6)alkyl; trifluoro-(C_1-C_6)-alkyl; C_3-C_7 cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted by C_1-C_6 alkyl, C_2-C_6 alkenyl, OH-(C_1-C_6)alkyl, or =O; C_2-C_6 alkenyl; R^{21}-aryl(C_1-C_6)alkyl; R^{21}-aryl-(C_2-C_6)-alkenyl; R^{21}-aryloxy; R^{21}-aryl-NH-; heteroaryl(C_1-C_6)alkyl; heteroaryl(C_2-C_6)-alkenyl; heteroaryloxy; heteroaryl-NH-; hydroxy(C_1-C_6)alkyl; dihydroxy(C_1-C_6)alkyl; amino(C_1-C_6)alkyl; (C_1-C_6)alkylamino-(C_1-C_6)alkyl; di-((C_1-C_6)alkyl)-amino(C_1-C_6)alkyl; thio(C_1-C_6)alkyl; C_1-C_6 alkoxy; C_2-C_6 alkenyloxy; halogen; -NR^4R^5; -CN; -OH; -$COOR^{17}$; -COR^{16}; -OSO_2CF_3; -$CH_2OCH_2CF_3$; (C_1-C_6)alkylthio; -$C(O)NR^4R^5$; -$OCHR^6$-phenyl; phenoxy-(C_1-C_6)alkyl; -$NHCOR^{16}$; -$NHSO_2R^{16}$; biphenyl; -$OC(R^6)_2COOR^7$; -$OC(R^6)_2C(O)NR^4R^5$; (C_1-C_6)alkoxy; -$C(=NOR^{17})R^{18}$; C_1-C_6 alkoxy substituted by (C_1-C_6)alkyl, amino, -OH, $COOR^{17}$, -$NHCOOR^{17}$, -$CONR^4R^5$, aryl, aryl substituted by 1 to 3 moieties independently selected from the group consisting of halogen, -CF_3, C_1-C_6 alkyl, C_1-C_6 alkoxy and -$COOR^{17}$, aryl wherein adjacent carbons form a ring with a methylenedioxy group, -$C(O)NR^4R^5$ or heteroaryl; R^{21}-aryl; aryl wherein adjacent carbons form a ring with a methylenedioxy group; R^{41}-heteroaryl; and heteroaryl wherein adjacent carbon atoms form a ring with a C_3-C_5 alkylene group or a methylenedioxy group;

R^4 and R^5 are independently selected from the group consisting of H, C_1-C_6 alkyl, phenyl, benzyl and C_3-C_7 cycloalkyl, or R^4 and R^5 together are -$(CH_2)_4$-, -$(CH_2)_5$- or -$(CH_2)_2NR^7$-$(CH_2)_2$- and form a ring with the nitrogen to which they are attached;

R^4 and R^5 are independently selected from the group consisting of H, C_1-C_6 alkyl, phenyl, benzyl and C_3-C_7 cycloalkyl, or R^4 and R^5 together are -$(CH_2)_4$-, -$(CH_2)_5$- or -$(CH_2)_2NR^7$-$(CH_2)_2$- and form a ring with the nitrogen to which they are attached;

R^6 is independently selected from the group consisting of H, C_1-C_6 alkyl, phenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl and amino(C_1-C_6)alkyl;

R^7 is H or (C_1-C_6)alkyl;

R^8, R^{10} and R^{11} are independently selected from the group consisting of R^1 and -OR^1, provided that when the optional double bond is present, R^{10} is absent;

R^9 is H, OH, C_1-C_6 alkoxy, halogen or halo(C_1-C_6)alkyl;

B is -$(CH_2)_{n3}$-, -CH_2-O-, -CH_2S-, -CH_2-NR^6-, -C(O)NR^6-, -NR^6C(O)-,

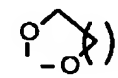
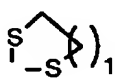
 , cis or trans -$(CH_2)_{n4}CR^{12}$=$CR^{12a}(CH_2)_{n5}$- or -$(CH_2)_{n4}$C≡C$(CH_2)_{n5}$-,

wherein n_3 is 0-5, n_4 and n_5 are independently 0-2, and R^{12} and R^{12a} are independently selected from the group consisting of H, C_1-C_6 alkyl and halogen;

X is -O- or -NR^6- when the double dotted lines adjacent to X represent a single bond, or X is H, -OH or -NHR^{20} when the bond is absent;

Y is =O, =S, (H, H), (H, OH) or (H, C_1-C_6 alkoxy) when the double dotted lines adjacent to X represent a single bond, or when the bond is absent, Y is =O, =NOR^{17}, (H, H), (H, OH), (H, SH), (H, C_1-C_6 alkoxy) or (H, -NHR^{45});

R^{15} is absent when the double dotted lines adjacent to X represent a single bond; R^{15} is H, C_1-C_6 alkyl, -$NR^{18}R^{19}$ or -OR^{17} when said single bond is absent; or

Y is  or  and R^{15} is H or C_1-C_6 alkyl;

R^{16} is C_1-C_6 lower alkyl, phenyl or benzyl;

R^{17}, R^{18} and R^{19} are independently selected from the group consisting of H, C_1-C_6 alkyl, phenyl, benzyl;

R^{20} is H, C_1-C_6 alkyl, phenyl, benzyl, -C(O)R^6 or -SO_2R^6;

R^{22} and R^{23} are independently selected from the group consisting of hydrogen, R^{24}-(C_1-C_{10})alkyl, R^{24}-(C_2-C_{10})alkenyl, R^{24}-(C_2-C_{10})alkynyl, R^{27}-hetero-cycloalkyl, R^{25}-aryl, R^{25}-aryl(C_1-C_6)alkyl, R^{29}-(C_3-C_7)cycloalkyl, R^{29}-(C_3-C_7)cycloalkenyl, -OH, -OC(O)R^{30}, -C(O)OR^{30}, -C(O)R^{30}, -C(O)N$R^{30}R^{31}$, -N$R^{30}R^{31}$, -NR^{30}C(O)R^{31}, -NR^{30}C(O)N$R^{31}R^{32}$, -NHSO_2R^{30}, -OC(O)N$R^{30}R^{31}$, R^{24}-(C_1-C_{10})alkoxy, R^{24}-(C_2-C_{10})-alkenyloxy, R^{24}-(C_2-C_{10})alkynyloxy, R^{27}-heterocycloalkyloxy, R^{29}-(C_3-C_7)cycloalkyloxy, R^{29}-(C_3-C_7)cyclo-alkenyloxy, R^{29}-(C_3-C_7)cycloalkyl-NH-, -CH_2-O-CH_2-phenyl, –NHSO_2NHR^{16} and–CH(=NOR^{17});

or R^{22} and R^{10} together with the carbon to which they are attached, or R^{23} and R^{11} together with the carbon to which they are attached, independently form a R^{42}-substituted carbocyclic ring of 3-10 atoms, or a R^{42}-substituted heterocyclic ring of 4-10 atoms wherein 1-3 ring members are independently selected from the group consisting of –O-, -NH- and –SO_{0-2}-, provided that when R^{22} and R^{10} form a ring, the optional double bond is absent;

R^{24} is 1, 2 or 3 moieties independently selected from the group consisting of hydrogen, halogen, -OH, (C_1-C_6)alkoxy, R^{35}-aryl, (C_1-C_{10})-alkyl-C(O)-, (C_2-C_{10})-alkenyl-C(O)-, (C_2-C_{10})alkynyl-C(O)-, heterocycloalkyl, R^{26}-(C_3-C_7)cycloalkyl, R^{26}-(C_3-C_7)cycloalkenyl, -OC(O)R^{30}, -C(O)OR^{30}, -C(O)R^{30}, -C(O)N$R^{30}R^{31}$, -N$R^{30}R^{31}$, -NR^{30}C(O)R^{31}, -NR^{30}C(O)N$R^{31}R^{32}$, -NHSO_2R^{30}, -OC(O)N$R^{30}R^{31}$, R^{24}-(C_2-C_{10})-alkenyloxy, R^{24}-(C_2-C_{10})alkynyloxy, R^{27}-heterocycloalkyloxy, R^{29}-(C_3-C_7)-cycloalkyloxy, R^{29}-(C_3-C_7)cyclo-alkenyloxy, R^{29}-(C_3-C_7)cycloalkyl-NH-, –NHSO_2NHR^{16} and –CH(=NOR^{17});

R^{25} is 1, 2 or 3 moieties independently selected from the group consisting of hydrogen, heterocycloalkyl, halogen, -COOR^{38}, -CN, -C(O)N$R^{37}R^{38}$, -NR^{39}C(O)R^{40}, -OR^{36}, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl-C_1-C_8)alkyl, (C_1-C_6)alkyl(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, halo(C_1-C_8)alkyl(C_3-C_7)cycloalkyl(C_1-C_6)alkyl, hydroxy(C_1-C_8)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, and R^{41}-heteroaryl; or two R^{25} groups on adjacent ring carbons form a fused methylenedioxy group;

R^{26} is 1, 2, or 3 moieties independently selected from the group consisting of hydrogen, halogen and (C_1-C_6)alkoxy;

R^{27} is 1, 2 or 3 moieties independently selected from the group consisting of hydrogen, R^{28}-(C_1-C_{10})alkyl, R^{28}-(C_2-C_{10})alkenyl, R^{28}-(C_2-C_{10})alkynyl;

R^{28} is hydrogen, -OH or (C_1-C_6)alkoxy;

R^{29} is 1, 2 or 3 moieties independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, -OH, (C_1-C_6)alkoxy and halogen;

R^{30}, R^{31} and R^{32} are independently selected from the group consisting of hydrogen, (C_1-C_{10})-alkyl, (C_1-C_6)alkoxy(C_1-C_{10})-alkyl, R^{25}-aryl(C_1-C_6)-alkyl, R^{33}-(C_3-C_7)cycloalkyl, R^{34}-(C_3-C_7)cycloalkyl(C_1-C_6)alkyl, R^{25}-aryl, heterocycloalkyl, heteroaryl, heterocycloalkyl(C_1-C_6)alkyl and heteroaryl(C_1-C_6)alkyl;

R^{33} is hydrogen, (C_1-C_6)alkyl, OH-(C_1-C_6)alkyl or (C_1-C_6)alkoxy;

R^{35} is 1 to 4 moieties independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, -OH, halogen, -CN, (C_1-C_6)alkoxy, trihalo(C_1-C_6)alkoxy, (C_1-C_6)alkylamino, di((C_1-C_6)alkyl)amino, -OCF_3, OH-(C_1-C_6)alkyl, -CHO, -C(O)(C_1-C_6)-alkylamino, -C(O)di((C_1-C_6)alkyl)amino, -NH_2, -NHC(O)(C_1-C_6)alkyl and -N((C_1-C_6)alkyl)C(O)(C_1-C_6)alkyl;

R^{36} is hydrogen, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, dihalo(C_1-C_6)alkyl or trifluoro(C_1-C_6)alkyl;

R^{37} and R^{38} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, aryl(C_1-C_6)alkyl, phenyl and (C_3-C_{15})cycloalkyl, or R^{37} and R^{38} together are –(CH_2)$_4$-, -(CH_2)$_5$- or –(CH_2)$_2$-NR^{39}-(CH_2)$_2$- and form a ring with the nitrogen to which they are attached;

R^{39} and R^{40} are independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, aryl(C_1-C_6)alkyl, phenyl and (C_3-C_{15})-cycloalkyl, or R^{39} and R^{40} in the group -NR^{39}C(O)R^{40}, together with the carbon and nitrogen atoms to which they are attached, form a cyclic lactam having 5-8 ring members;

R^{41} is 1 to 4 moieties independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkylamino, di((C_1-C_6)alkyl)amino, -OCF_3, OH-(C_1-C_6)alkyl, -CHO and phenyl;

R^{42} is 1 to 3 moieties independently selected from the group consisting of hydrogen, -OH, (C_1-C_6)alkyl and (C_1-C_6)alkoxy;

R^{43} is -$NR^{30}R^{31}$, -NR^{30}C(O)R^{31}, -NR^{30}C(O)$NR^{31}R^{32}$, -$NHSO_2R^{30}$ or –$NHCOOR^{17}$;

R^{44} is H, C_1-C_6 alkoxy, -SOR^{16}, -SO_2R^{17}, -C(O)OR^{17}, -C(O)$NR^{18}R^{19}$, C_1-C_6 alkyl, halogen, fluoro(C_1-C_6)alkyl, difluoro(C_1-C_6)alkyl, trifluoro(C_1-C_6)alkyl, C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, aryl(C_1-C_6)alkyl, aryl(C_2-C_6)alkenyl, heteroaryl(C_1-C_6)alkyl, heteroaryl(C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl or (C_1-C_6)alkylamino(C_1-C_6)alkyl; and

R^{45} is H, C_1-C_6 alkyl, -$COOR^{16}$ or -SO_2,

wherein said therapeutic condition is a cardiovascular or circulatory disease or condition, an inflammatory disease or condition, a respiratory tract disease or condition, cancer, acute renal failure, glomerulonephritis, astrogliosis, a fibrotic disorder of the liver, kidney, lung or intestinal tract, Alzheimer's disease, diabetes, diabetic neuropathy, rheumatoid arthritis, neurodegenerative disease, neurotoxic disease, systemic lupus erythematosus, multiple sclerosis, osteoporosis, glaucoma, macular degeneration, psoriasis, radiation fibrosis, endothelial dysfunction, a wound or a spinal cord injury, or a symptom or result thereof.

2. (Previously presented) The method of claim 1 wherein the cardiovascular or circulatory disease or condition is atherosclerosis, restenosis, hypertension, acute coronary syndrome, angina pectoris, arrhythmia, heart disease, heart failure, myocardial infarction, thrombotic or thromboembolytic stroke, a peripheral vascular disease, deep vein thrombosis, venous thromboembolism, a cardiovascular disease associated with hormone replacement therapy, disseminated intravascular coagulation syndrome, renal ischemia, cerebral stroke, cerebral ischemia, cerebral infarction, migraine, renal vascular homeostasis or erectile dysfunction.

3. (Currently amended) The method of claim 1 wherein the inflammatory disease or condition is irritable bowel syndrome, Crohn's disease, nephritis or a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder, ~~gastrointestinal tract~~ or other organ.

4. (Previously presented) The method of claim 1 wherein the respiratory tract disease or condition is reversible airway obstruction, asthma, chronic asthma, bronchitis or chronic airways disease.

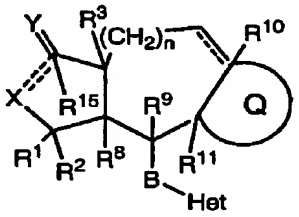
5. (Previously presented) The method of claim 1 wherein the cancer is renal cell carcinoma or an angiogenesis related disorder.

6. (Previously presented) The method of claim 1 wherein the neurodegenerative disease is Parkinson's disease, amyotropic lateral sclerosis, Alzheimer's disease, Huntington's disease or Wilson's disease.

7. (Previously presented) The method of claim 1 further comprising administering at least one therapeutically effective agent useful in the treatment of inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, neuropathy and/or malignant tumors, angiogenesis related disorders, cancer, disorders of the liver, kidney or lung, melanoma, renal cell carcinoma, renal disease, acute renal failure, chronic renal failure, renal vascular homeostasis, glomerulonephritis, chronic airways disease, bladder inflammation, neurodegenerative and/or neurotoxic diseases, conditions, or injuries, radiation fibrosis, endothelial dysfunction, periodontal diseases or wounds.

8. (Previously presented) The method of claim 7 further comprising administering at least two therapeutically effective agents.

9. (Previously presented) A method of treating a therapeutic condition comprising administering to a mammal in need of such treatment an effective amount of at least one compound of the formula:



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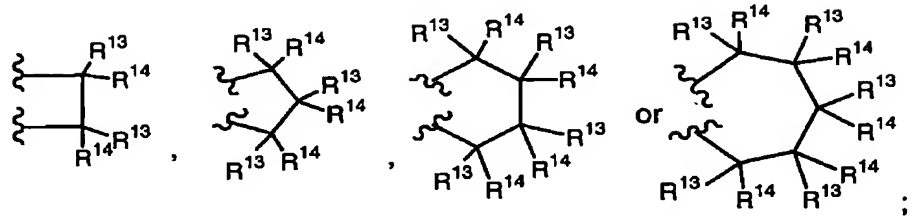
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof, wherein:

the double dotted lines adjacent to X ====== together represent an optional single bond;

the single dotted line adjacent to R^{10} ====== represents an optional double bond;

n is 0-2;

Q is



R^1 and R^2 are independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, fluoro$(C_1\text{-}C_6)$alkyl-, difluoro$(C_1\text{-}C_6)$alkyl-, trifluoro-$(C_1\text{-}C_6)$alkyl-, $(C_3\text{-}C_6)$cycloalkyl, $(C_2\text{-}C_6)$alkenyl, hydroxy-$(C_1\text{-}C_6)$alkyl-, and amino$(C_1\text{-}C_6)$alkyl-;

R^3 is H, hydroxy, $(C_1\text{-}C_6)$alkoxy, $-SOR^{16}$, $-SO_2R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{18}R^{19}$, $-(C_1\text{-}C_6)$alkyl-$C(O)NR^{18}R^{19}$, $(C_1\text{-}C_6)$alkyl, halogen, fluoro$(C_1\text{-}C_6)$alkyl-, difluoro$(C_1\text{-}C_6)$alkyl-, trifluoro$(C_1\text{-}C_6)$alkyl-, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$-cycloalkyl-$(C_1\text{-}C_6)$alkyl-, $(C_2\text{-}C_6)$alkenyl, aryl$(C_1\text{-}C_6)$alkyl-, aryl$(C_2\text{-}C_6)$alkenyl-, heteroaryl$(C_1\text{-}C_6)$alkyl-, heteroaryl$(C_2\text{-}C_6)$alkenyl-, hydroxy$(C_1\text{-}C_6)$-alkyl-, $-NR^{22}R^{23}$, $NR^{22}R^{23}$-$(C_1\text{-}C_6)$alkyl-, aryl, thio$(C_1\text{-}C_6)$alkyl-, $(C_1\text{-}C_6)$alkyl-thio$(C_1\text{-}C_6)$alkyl-, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl-, $NR^{18}R^{19}$-C(O)-$(C_1\text{-}C_6)$alkyl- or $(C_3\text{-}C_6)$cycloalkyl-$(C_1\text{-}C_6)$alkyl-;

Het is a mono- or bi-cyclic heteroaryl group of 5 to 10 atoms comprised of 1 to 9 carbon atoms and 1 to 4 heteroatoms independently selected from the group consisting of N, O and S, wherein a ring nitrogen can form an N-oxide or a quaternary group with a $(C_1\text{-}C_4)$alkyl group, wherein Het is attached to B by a carbon atom ring member of said Het, and wherein the Het group is substituted by W;

W is 1 to 4 moieties independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, fluoro$(C_1\text{-}C_6)$alkyl-, difluoro$(C_1\text{-}C_6)$alkyl-, trifluoro$(C_1\text{-}C_6)$alkyl-, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_1\text{-}C_6)$alkyl-, dihydroxy$(C_1\text{-}C_6)$alkyl-, $NR^{25}R^{26}(C_1\text{-}C_6)$alkyl-, thio$(C_1\text{-}C_6)$alkyl-, -OH, $(C_1\text{-}C_6)$alkoxy, halogen, $-NR^4R^5$, $-C(O)OR^{17}$, $-COR^{16}$, $(C_1\text{-}C_6)$alkylthio-, R^{21}-aryl, R^{21}-aryl$(C_1\text{-}C_6)$alkyl-, aryl wherein adjacent ring carbons in said aryl, along with two O atoms, form a methylenedioxy group, and R^{21}-heteroaryl;

R^4 and R^5 are independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, phenyl, benzyl and $(C_3\text{-}C_6)$cycloalkyl, or R^4 and R^5 taken together are $-(CH_2)_4$-, $-(CH_2)_5$- or $-(CH_2)_2NR^7(CH_2)_2$- and form a ring with the nitrogen to which they are attached;

R^6 is H, $(C_1\text{-}C_6)$alkyl or phenyl;

R^7 is H, $(C_1\text{-}C_6)$alkyl, -C(O)-R^{16}, -C(O)OR^{17} or $-S(O)_2R^{17}$;

R^8, R^{10} and R^{11} are independently selected from the group consisting of R^1 and $-OR^1$, provided that when the optional double bond shown in Formula II is present, R^{10} is absent;

R^9 is H, OH or $(C_1\text{-}C_6)$alkoxy;

B is $-(CH_2)_{n3}-$, cis or trans $-(CH_2)_{n4}CR^{12}=CR^{12a}(CH_2)_{n5}-$ or $-(CH_2)_{n4}C\equiv C(CH_2)_{n5}-$, wherein n_3 is 0-5, n_4 and n_5 are independently 0-2, and R^{12} and R^{12a} are independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl and halogen;

X is -O- or $-NR^6-$ when the dotted line shown adjacent to X in Formula II represents a single bond, or X is -OH or $-NHR^{20}$ when the bond is absent;

Y is =O, =S, (H, H), (H, OH) or (H, $(C_1\text{-}C_6)$alkoxy) when the dotted line shown adjacent to X in Formula II represents a single bond, or when the bond is absent, Y is =O, (H, H), (H, OH), (H, SH) or (H, $(C_1\text{-}C_6)$alkoxy);

each R^{13} is independently selected from H, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $-(CH_2)_{n6}NHC(O)OR^{16b}$, $-(CH_2)_{n6}NHC(O)R^{16b}$, $-(CH_2)_{n6}NHC(O)NR^4R^5$, $-(CH_2)_{n6}NHSO_2R^{16}$, $-(CH_2)_{n6}NHSO_2NR^4R^5$, and $-(CH_2)_{n6}C(O)NR^{28}R^{29}$ where n_6 is 0-4, haloalkyl, and halogen;

each R^{14} is independently selected from H, $(C_1\text{-}C_6)$alkyl, -OH, $(C_1\text{-}C_6)$alkoxy, R^{27}-aryl$(C_1\text{-}C_6)$alkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocyclylalkyl, $-(CH_2)_{n6}NHC(O)OR^{16b}$, $-(CH_2)_{n6}NHC(O)R^{16b}$, $-(CH_2)_{n6}NHC(O)NR^4R^5$, $-(CH_2)_{n6}NHSO_2R^{16}$, $-(CH_2)_{n6}NHSO_2NR^4R^5$, and $-(CH_2)_{n6}C(O)NR^{28}R^{29}$ where n_6 is 0-4, halogen and haloalkyl; or

R^{13} and R^{14} taken together form a spirocyclic or a heterospirocyclic ring of 3-6 atoms;

wherein at least one of R^{13} or R^{14} is selected from the group consisting of $-(CH_2)_{n6}NHC(O)OR^{16b}$, $-(CH_2)_{n6}NHC(O)R^{16b}$, $-(CH_2)_{n6}NHC(O)NR^4R^5$, $-(CH_2)_{n6}NHSO_2R^{16}$, $-(CH_2)_{n6}NHSO_2NR^4R^5$, and $-(CH_2)_{n6}C(O)NR^{28}R^{29}$ where n_6 is 0-4;

R^{15} is H when the double dotted line shown adjacent to X in Formula II represents a single bond and is H, $(C_1\text{-}C_6)$alkyl, $-NR^{18}R^{19}$, or $-OR^{17}$ when said bond is absent;

R^{16} is independently selected from the group consisting of $(C_1\text{-}C_6)$alkyl, phenyl and benzyl;

R^{16b} is H, alkoxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl-, R^{22}-O-C(O)-(C_1-C_6)alkyl-, (C_3-C_8)cycloalkyl, R^{21}-aryl, R^{21}-aryl(C_1-C_6)alkyl, haloalkyl, alkenyl, halosubstituted alkenyl, alkynyl, halosubstituted alkynyl, R^{21}-heteroaryl, R^{21}-(C_1-C_6)alkyl heteroaryl, R^{21}-(C_1-C_6)alkyl heterocycloalkyl, $R^{28}R^{29}$N-(C_1-C_6)alkyl, $R^{28}R^{29}$N-(CO)-(C_1-C_6)alkyl, $R^{28}R^{29}$N-(CO)O-(C_1-C_6)alkyl, R^{28}O(CO)N(R^{29})-(C_1-C_6)alkyl, $R^{28}S(O)_2N(R^{29})$-(C_1-C_6)alkyl, $R^{28}R^{29}$N-(CO)-N(R^{29})- (C_1-C_6)alkyl, $R^{28}R^{29}$N-S(O)2N(R^{29})-(C_1-C_6)alkyl, R^{28}-(CO)N(R^{29})-(C_1-C_6)alkyl, $R^{28}R^{29}$N-$S(O)_2$-(C_1-C_6)alkyl, $HOS(O)_2$-(C_1-C_6)alkyl, $(OH)_2P(O)_2$-(C_1-C_6)alkyl, R^{28}-S-(C_1-C_6)alkyl, R^{28}-$S(O)_2$-(C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl);

R^{17}, R^{18} and R^{19} are independently selected from the group consisting of H, (C_1-C_6)alkyl, phenyl, and benzyl;

R^{20} is H, (C_1-C_6)alkyl, phenyl, benzyl, -C(O)R^6 or $-S(O)_2R^6$;

R^{21} is 1 to 3 moieties independently selected from the group consisting of H, -CN, $-CF_3$, $-OCF_3$, halogen, $-NO_2$, (C_1-C_6)alkyl, -OH, (C_1-C_6)alkoxy, (C_1-C_6)-alkylamino-, di-$((C_1-C_6)$alkyl)amino-, $NR^{25}R^{26}$-(C_1-C_6)alkyl-, hydroxy-(C_1-C_6)alkyl-,-C(O)OR^{17}, -C(O)R^{17}, -NHC(O)R^{16}, $-NHS(O)_2R^{16}$, $-NHS(O)_2CH_2CF_3$, -C(O)$NR^{25}R^{26}$, -NR^{25}-C(O)-$NR^{25}R^{26}$, -S(O)R^{13}, $-S(O)_2R^{13}$ and $-SR^{13}$;

R^{22} is H or (C_1-C_6)alkyl;

R^{23} is H, (C_1-C_6)alkyl, -C(O)R^{24}, $-S(O)_2R^{24}$, -C(O)NHR^{24} or $-S(O)_2NHR^{24}$;

R^{24} is (C_1-C_6)alkyl, hydroxy (C_1-C_6)alkyl or $NR^{25}R^{26}$-$((C_1-C_6)$alkyl)-;

R^{25} and R^{26} are independently selected from the group consisting of H and (C_1-C_6)alkyl;

R^{27} is 1, 2 or 3 moieties selected from the group consisting of H, (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, (C_1-C_6)alkoxy, halogen and –OH; and

R^{28} and R^{29} are independently selected from the group consisting of H, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, R^{27}-aryl(C_1-C_6)alkyl, heteroaryl, heteroarylalkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, heterocyclyl, heterocyclylalkyl, and haloalkyl; or

R^{28} and R^{29} taken together form a spirocyclic or a heterospirocyclic ring of 3-6 atoms,

wherein said therapeutic condition is a cardiovascular or circulatory disease or condition, an inflammatory disease or condition, a respiratory tract disease or

condition, cancer, acute renal failure, glomerulonephritis, astrogliosis, a fibrotic disorder of the liver, kidney, lung or intestinal tract, Alzheimer's disease, diabetes, diabetic neuropathy, rheumatoid arthritis, neurodegenerative disease, neurotoxic disease, systemic lupus erythematosus, multiple sclerosis, osteoporosis, glaucoma, macular degeneration, psoriasis, radiation fibrosis, endothelial dysfunction, a wound or a spinal cord injury, or a symptom or result thereof.

10. (Previously presented) The method of claim 9 wherein the cardiovascular or circulatory disease or condition is atherosclerosis, restenosis, hypertension, acute coronary syndrome, angina pectoris, arrhythmia, heart disease, heart failure, myocardial infarction, thrombotic or thromboembolytic stroke, a peripheral vascular disease, deep vein thrombosis, venous thromboembolism, a cardiovascular disease associated with hormone replacement therapy, disseminated intravascular coagulation syndrome, renal ischemia, cerebral stroke, cerebral ischemia, cerebral infarction, migraine, renal vascular homeostasis or erectile dysfunction.

11. (Currently amended) The method of claim 9 wherein the inflammatory disease or condition is irritable bowel syndrome, Crohn's disease, nephritis or a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder, ~~gastrointestinal tract~~ or other organ.

12. (Previously presented) The method of claim 9 wherein the respiratory tract disease or condition is reversible airway obstruction, asthma, chronic asthma, bronchitis or chronic airways disease.

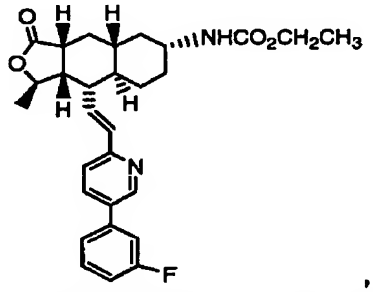
13. (Previously presented) The method of claim 9 wherein the cancer is renal cell carcinoma or an angiogenesis related disorder.

14. (Previously presented) The method of claim 9 wherein the neurodegenerative disease is Parkinson's disease, amyotropic lateral sclerosis, Alzheimer's disease, Huntington's disease or Wilson's disease.

15. (Previously presented) The method of claim 9 further comprising administering at least one therapeutically effective agent useful in the treatment of inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, neuropathy and/or malignant tumors, angiogenesis related disorders, cancer, disorders of the liver, kidney or lung, melanoma, renal cell carcinoma, renal disease, acute renal failure, chronic renal failure, renal vascular homeostasis, glomerulonephritis, chronic airways disease, bladder inflammation, neurodegenerative and/or neurotoxic diseases, conditions, or injuries, radiation fibrosis, endothelial dysfunction, periodontal diseases or wounds.

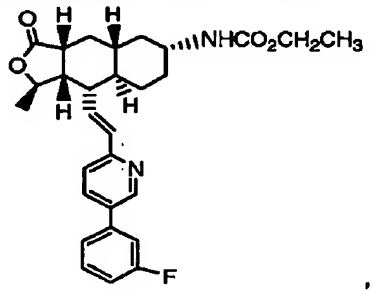
16. (Previously presented) The method of claim 15 further comprising administering at least two therapeutically effective agents.

17. (New) The method of claim 9 wherein said compound is



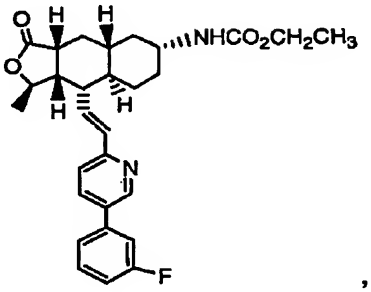
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

18. (New) The method of claim 10 wherein said compound is



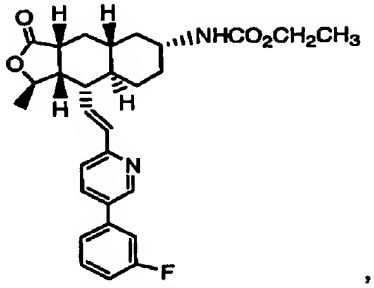
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

19. (New) The method of claim 11 wherein said compound is



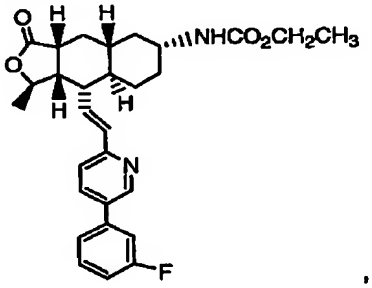
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

20. (New) The method of claim 12 wherein said compound is



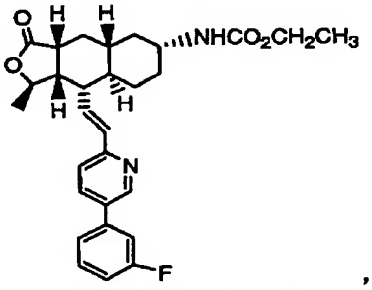
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

21. (New) The method of claim 13 wherein said compound is



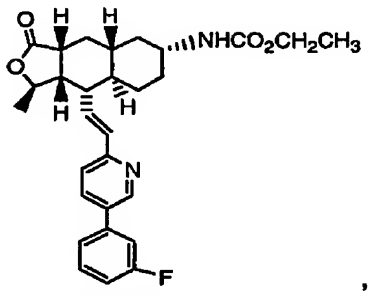
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

22. (New) The method of claim 14 wherein said compound is



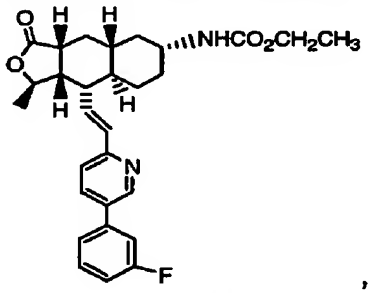
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

23. (New) The method of claim 15 wherein said compound is



or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

24. (New) The method of claim 16 wherein said compound is



or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

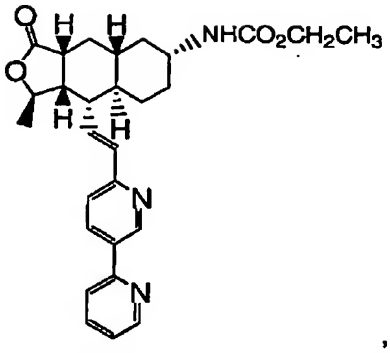
25. (New) The method of claim 17 wherein said inflammatory disease or condition is irritable bowel syndrome, Crohn's disease, nephritis or a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder or other organ.

26. (New) The method of claim 17 wherein said inflammatory disease or condition is a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder or other organ.

27. (New) The method of claim 17 wherein said inflammatory disease or condition is a radiation- induced proliferative or inflammatory disorder of the gastrointestinal tract.

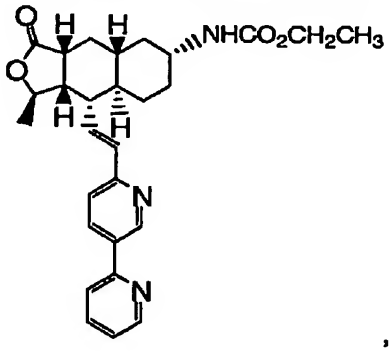
28. (New) The method of claim 17 wherein said cardiovascular or circulatory disease or condition is acute coronary syndrome.

29. (New) The method of claim 9 wherein said compound is



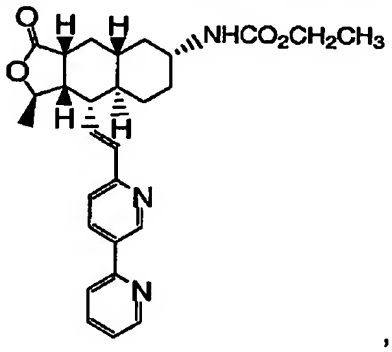
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

30. (New) The method of claim 10 wherein said compound is



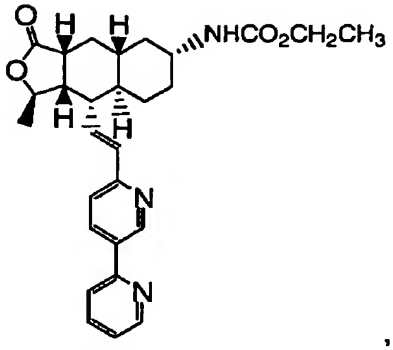
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

31. (New) The method of claim 11 wherein said compound is



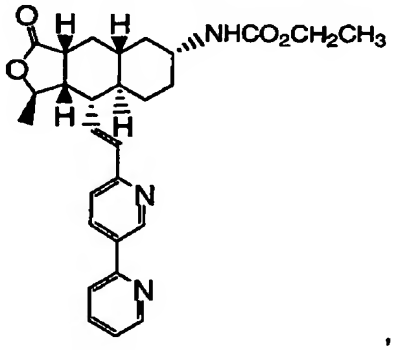
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

32. (New) The method of claim 12 wherein said compound is



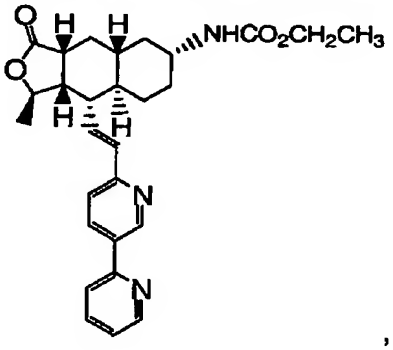
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

33. (New) The method of claim 13 wherein said compound is



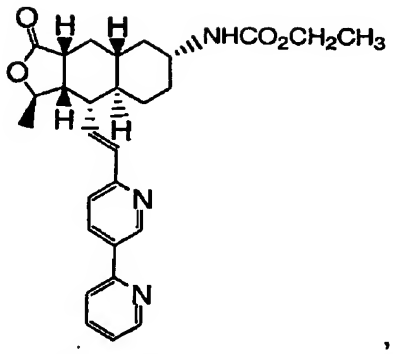
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

34. (New) The method of claim 14 wherein said compound is



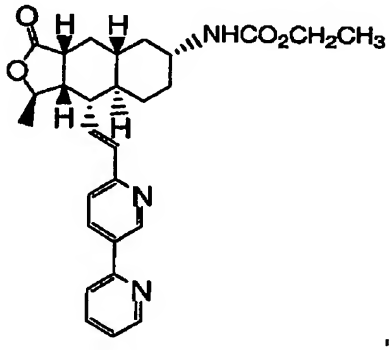
or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

35. (New) The method of claim 15 wherein said compound is



or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

36. (New) The method of claim 16 wherein said compound is



or a pharmaceutically acceptable isomer, salt, solvate or co-crystal form thereof.

37. (New) The method of claim 29 wherein said inflammatory disease or condition is irritable bowel syndrome, Crohn's disease, nephritis or a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder or other organ.

38. (New) The method of claim 29 wherein said inflammatory disease or condition is a radiation- or chemotherapy- induced proliferative or inflammatory disorder of the gastrointestinal tract, lung, urinary bladder or other organ.

39. (New) The method of claim 29 wherein said inflammatory disease or condition is a radiation-induced proliferative or inflammatory disorder of the gastrointestinal tract.